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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,527	OLANDT ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *8-11,13-17 and 19-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,12,18 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10-24-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-27 are currently pending and are present for examination. Claims 1-7, 12, 18, 25-27 are now under consideration. Claims 8-11, 13-17, 19-24 remain withdrawn from consideration as being drawn to non-elected subject matter.

Election/Restrictions

Applicant's election of Group I in Paper filed on 11-17-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawing submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because of the following informalities: There are several blank spaces in the specification with incomplete information. For example see page 2 while reciting ATCC accession number. Appropriate correction is required.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5-7, 25-26 are rejected under 35 U.S.C. 101 because the claimed invention appears to be directed to non-statutory subject matter. Claims 5-7, 25-26 are drawn to host cells which expresses or contains the nucleic acid of claim 1. Such claims read on all naturally occurring cells that express or contain the polynucleotide of claim 1. Even though the polynucleotide of claim 1 is drawn to an isolated polynucleotide, the claim could be broadly interpreted as reading on natural cells expressing or simply containing said polynucleotide. Amending the claim to recite "a recombinant host cell transformed with the nucleic acid of claim 1" or "a host cell transformed with the polynucleotide of claim 1" to clearly show the hand of man would overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-7, 12, 18, 25-26 all of which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "simple sugar". The metes and bounds of this phrase is not clear to the Examiner. A perusal of the specification did not provide a specific group of sugars that the applicant considers as simple sugars. Examiner was unable to find a clear definition for said phrase in the art as well. Therefore, the above phrase renders the claim indefinite.

Claim 1 and claims 2-7, 12, 18, 25-26 all of which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "target molecule". The metes and bounds of this phrase is not clear to the Examiner. It is not clear to the Examiner as to what molecules, applicant considers as target molecule. A perusal of the specification did not provide a specific group of molecules that the applicant considers as target molecules. Examiner was unable to find a clear definition for said phrase in the art as well. Therefore, the above phrase renders the claim indefinite.

Claim 1 and claims 2-7, 12, 18, 25-26 all of which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "a membrane". The metes and bounds of this phrase is not clear to the Examiner. It is not clear to the Examiner as to what are all the types of membranes that are encompassed in the

claim. A perusal of the specification did not provide any specific type of membrane such as the cell membrane, nuclear membrane or Golgi membrane, organic polymer membrane, latex membrane, artificial liposomal membrane etc. that the applicant considers as "membranes". Examiner was unable to find a clear definition for said phrase in the art as well. Therefore, the above phrase renders the claim indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and claims 2-7, 12, 18, 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide with SEQ ID NO:2 and having a specific glycosyltransferase activity (i.e., transfer sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid), vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide, does not reasonably provide enablement for any such polynucleotide which is at least 90% identical to SEQ ID NO:1 or 3 and encoding a polypeptide with that has at least one activity selected from the group consisting of ability to glycosylate (i.e., transfer of any sugar from any donor) a target molecule (any type of molecule), the ability to bind to simple sugar (when the definition of simple sugar is not clear) and the ability to attach to a membrane (when the definition of "membrane" is not clear), vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1 and claims 2-7, 12, 18, 25-26 are so broad as to encompass any polynucleotide that is at least 90% identical in its sequence to SEQ ID NO:1 or 3 and wherein said polynucleotide encodes a polypeptide not with any specific activity but with a broad activity of glycosylating (in any manner) a target molecule or simply binding to a simple sugar or have ability to bind to a membrane (see above), followed by vectors and host cells comprising such polynucleotides and method of making the polypeptide using such polynucleotides. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. Simply put, applicants have not taught those skilled in the art as

to where exactly on the polynucleotide sequence of SEQ ID NO:1 or 3 specific nucleotides can be modified (i.e., by insertion, deletion or substitution), and how to select those modified sequences in order to arrive at those that encode the polypeptide having the specific activity of SEQ ID NO:2. Furthermore, it would also require undue experimentation by those skilled in the art to use polynucleotides encoding polypeptide with such a vague or highly broad activities such as glycosylate target molecule without knowing what type of sugar is transferred to what type of "target" molecule. Similarly it would be an undue burden to those skilled in the art to use the claimed polynucleotide without knowing how to use the encoded polypeptide that simply binds to "simple sugars" or "membranes". The specification is limited to teaching the use of the polynucleotide with SEQ ID NO:1 or 3 to encode the polypeptide SEQ ID NO:2 and use it as a specific glycosyltransferase capable of transferring sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid but provides no guidance with regard to the making of variants and mutants or with regard to the other uses indicated above. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotide sequence leading to variants or mutants through which amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any encoded protein, and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with 90% identity to polynucleotides of SEQ ID NOS:1 and 3 because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without affecting its activity of encoding the polypeptide having the specific glycosyltransferase activity; (B) the general tolerance of polynucleotides encoding such glycosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide on the polynucleotide with an expectation of obtaining the desired biological function; (D) specific uses for polypeptides having the activity of binding to "simple sugars" or "membranes" encoded by the claimed polynucleotides and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful .

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides with an enormous number of nucleotide

modifications to SEQ ID NOS: 1 and 3 and the broad type of uses for the encoded polypeptides. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 1 and claims 2-7, 12, 18, 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules having the limitations of encoding a polypeptide having a large number of vague functions, such as ability to glycosylate (i.e., transfer of any sugar from any donor) a target molecule (any type of molecule), the ability to bind to simple sugar (when the definition of simple sugar is not clear) and the ability to attach to a membrane (when the definition of "membrane" is not clear), vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide.

While the specification does contain the structure of a couple of polynucleotides encoding a polypeptide having a specific function (transferring sugar from UDP-glucose, UDP-N-acetylgalactosamine, GDP-mannose or CDP-abequose to substrates such as cellulose, dolichol phosphate and teichoic acid), the specification does not contain any disclosure of the structure of all DNA sequences that have the limitations of encoding a polypeptide with a large number of

vague functions, such as ability to glycosylate (i.e., transfer of any sugar from any donor) a target molecule (any type of molecule), the ability to bind to simple sugar (when the definition of simple sugar is not clear) and the ability to attach to a membrane (when the definition of "membrane" is not clear), vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide. The genus of DNAs that comprise these above DNA molecules is a large variable genus having different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a couple of species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim 1 and claims 2-7, 12, 18, 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1 and 12 are specifically directed to a genus of DNA molecules with either SEQ ID NO:1 or 3 or naturally occurring

allelic variant polynucleotide sequence capable of hybridizing to SEQ ID NO:1 or 3 under stringent conditions.

The art defines an "allelic sequence" as an alternative form of the gene which may result in at least one mutation in the nucleic acid sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. This definition does not provide any specific information about the structure of naturally occurring (alleles) variants of SEQ ID NO:2 (i.e. where are the regions within which mutations are likely to occur). There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO:2 relates to the structure of any naturally occurring alleles. The general knowledge in the art concerning alleles dose not provide any indication of how one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art structure of one does not provide guidance to the structure of others. The genus of DNAs that comprise the claimed DNA molecules is a large variable genus with potentiality of having different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims. The specification discloses only a couple of species of the claimed genus (i.e. the sequence SEQ ID NO:1 and 3 encoding SEQ ID NO:2) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 12, 18, 25-27 are rejected under 35 U.S.C. 102(e) as being anticipated by either Sanjanwala et al. (WO02/46426 A2, June, 2002, with US priority date Dec 2000 to 02 Feb 2001) or Clausen et al. (US Pub 20020186850A1, Oct 2003, with US priority date May 2000). This rejection is based upon the public availability of a printed publications. Claims 1-7, 12, 18, 25-27 of the instant application are drawn to polynucleotides with SEQ ID NO:1 or 3 or those that have a sequence identity of at least 90% with SEQ ID NO:1 or 3 or polynucleotides that are allelic variants of the above encoding a polypeptide with SEQ ID NO:2 and having a specific glycosyltransferase activity, vectors and host cells comprising said polynucleotide and a method of making the polypeptide using the host cell comprising said polynucleotide. Sanjanwala et al. disclose polynucleotides that have a 100% sequence identity with SEQ ID NO :1 or 3 encoding a polypeptide with SEQ ID NO:2 and having a glycosyltransferase activity (see enclosed sequence alignments), vectors and host cells and method of making the polypeptide. On similar lines

Hassan et al. also disclose polynucleotides capable of hybridizing to SEQ ID NO:1 or 3 under stringent conditions and encode a polypeptide that is 98.5% identical to SEQ ID NO:2 which can be considered as an allelic variant or a variant of SEQ ID NO:2, vectors and host cells and method of making said polypeptide. Thus, Sanjanwala et al. or Clausen et al. anticipate claims 1-7, 12, 18, 25-27 of this application as written.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
January 18, 2004